Armed Forces College of Medicine

AFCM

كلية الطب بالقوات المسلحة

Armed Forces College of Medicine

The Complement system

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ILOs of Immunogens,Antigens & Self molecules

By the end of this lecture the student will be able to:

1. Compare between the 3 pathways of complement activation

2- Describe the biological effects of complement

3.Outline the importance and mechanisms of complement regulation

COMPLEMENT SYSTEM

➲ Components

9 basic proteins : C1-C9

Others

Factors B,D,Properdin

➲ Source

Liver

➲ Site

Serum & tissue fluids

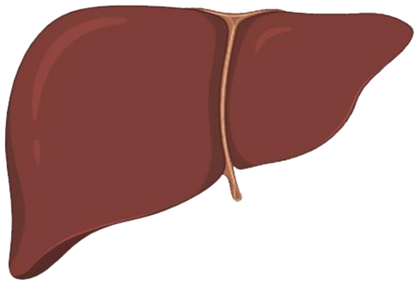
(except CSF & urine)

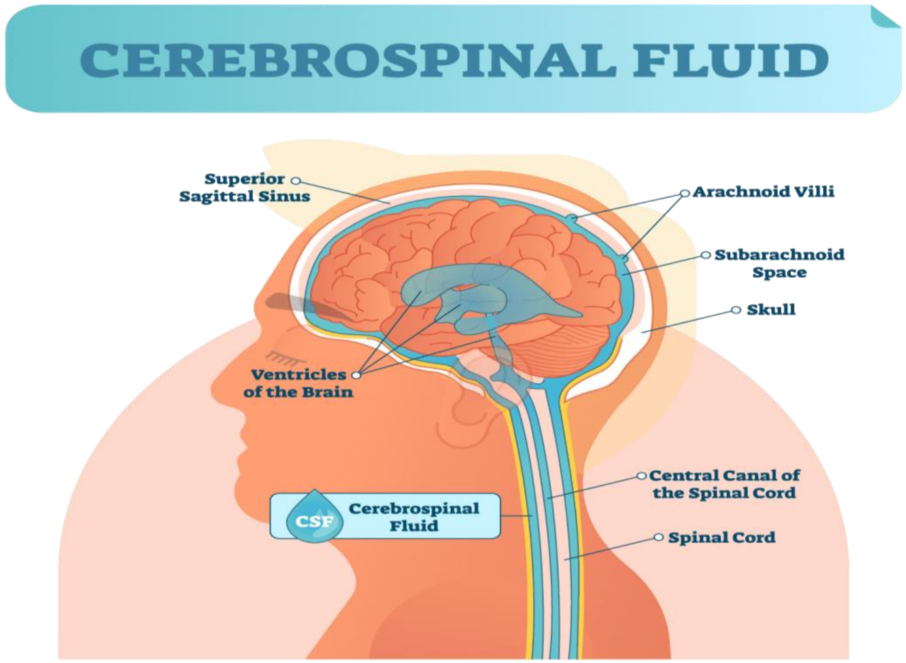
➲ Activation

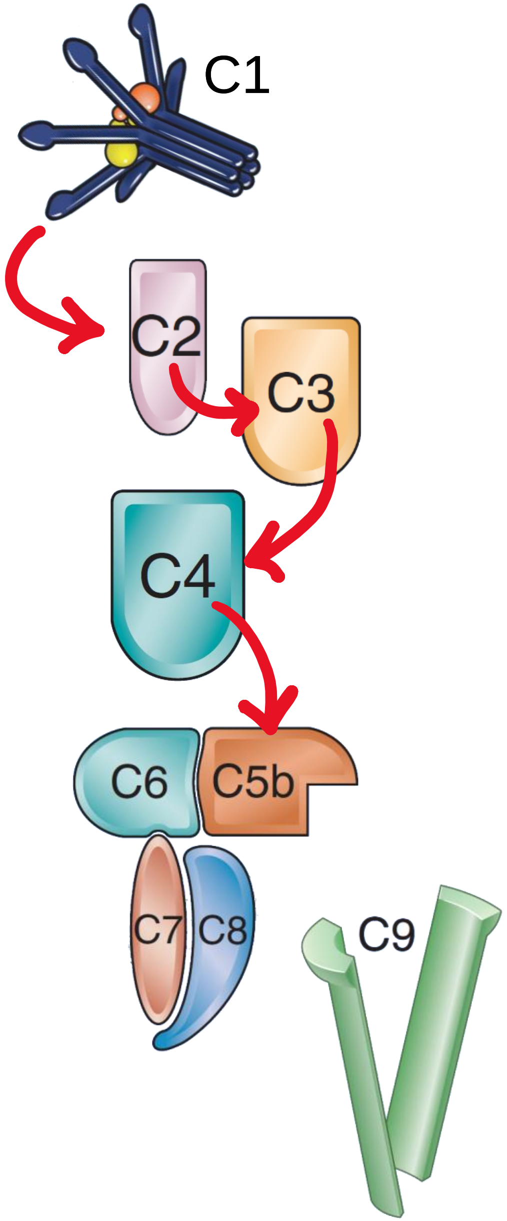
Circulate in inactive form

↓

⊕ in cascade manner





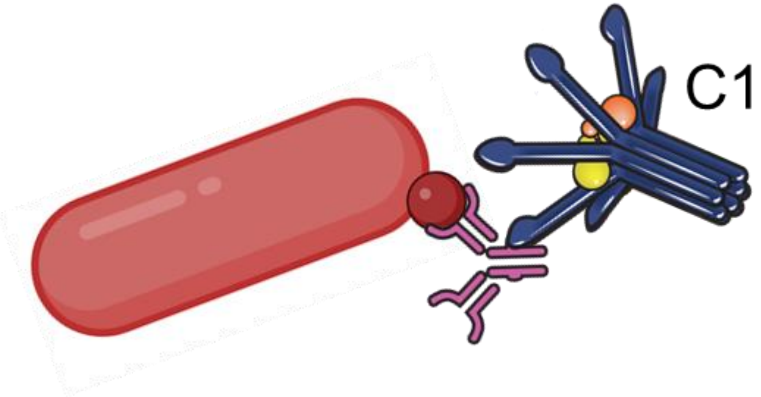


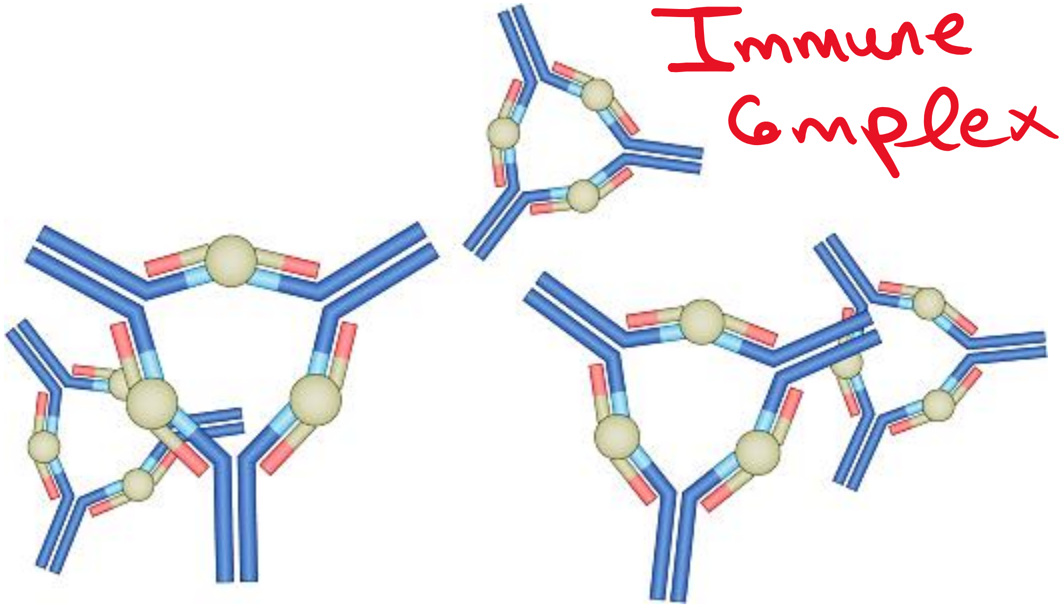
COMPLEMENT SYSTEM

Functions

1) Defense against microbes

2) Removal of immune complexes





Immune Complex

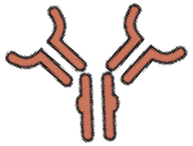
Classical pathway

Lectin pathway

Alternative pathway

Antibody dependent

(adaptive immunity)

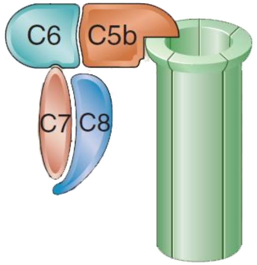


Antibody independent

(Innate immunity)

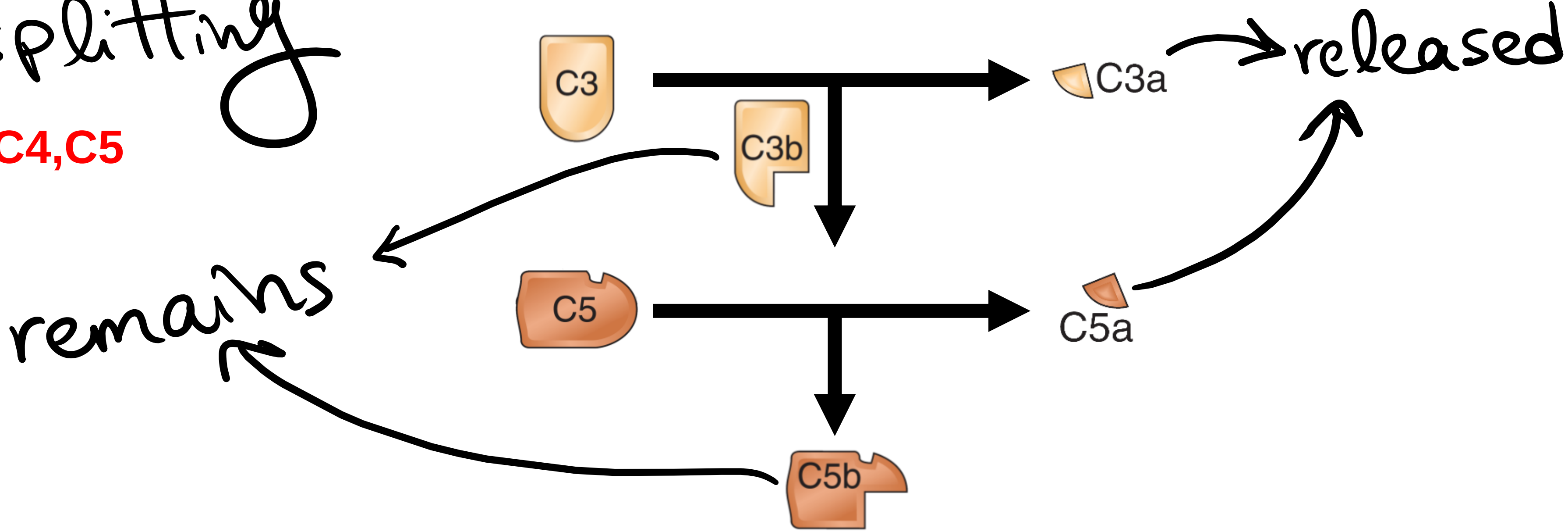
Generation of membrane attack complex (MAC):

C5b6789 (Common final pathway)



splitting

C2,C3,C4,C5



Classical pathway

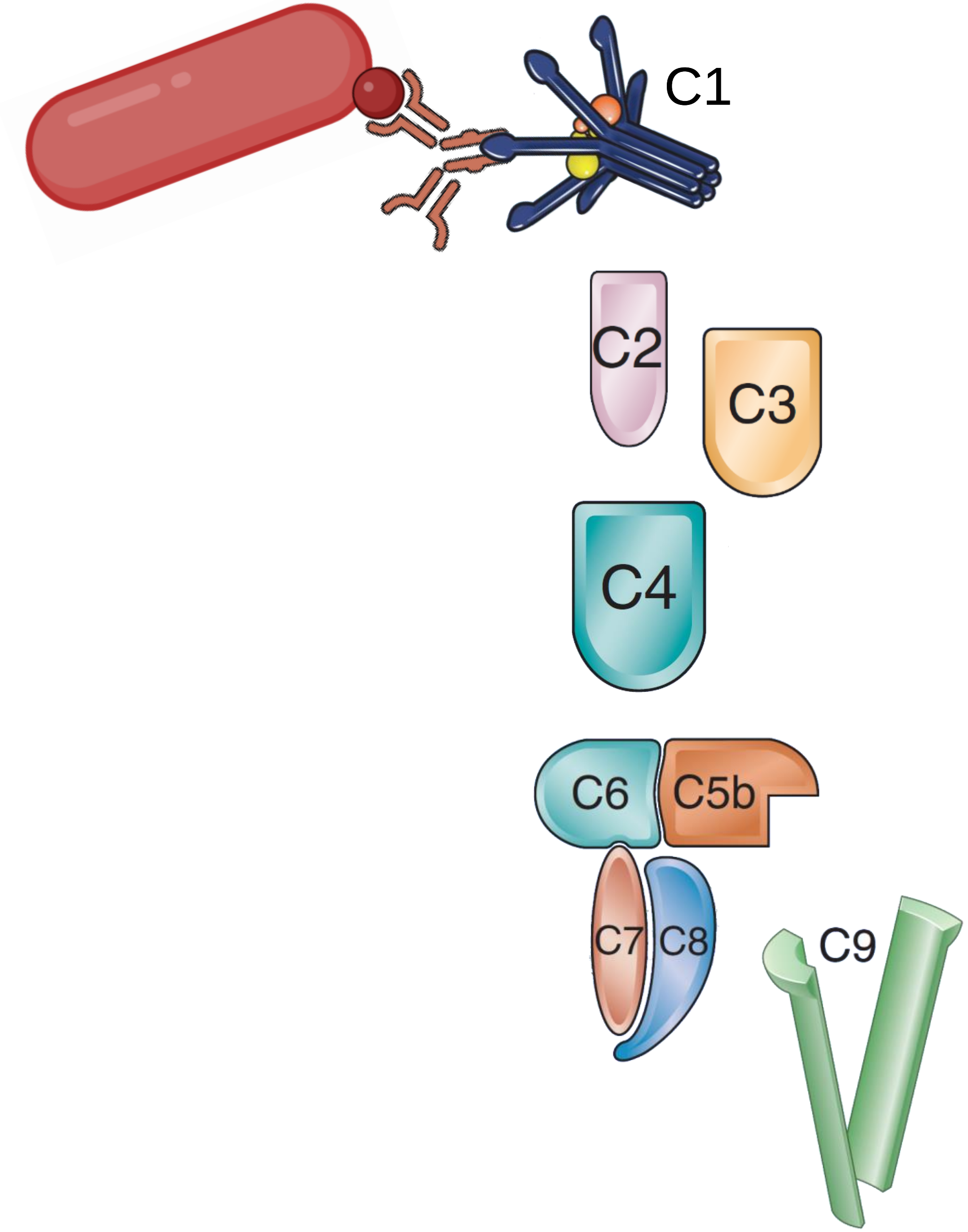
➲ Type of immunity

Humoral (Adaptive) immunity

By Ag-Ab complex

➲ Involved Components

C1 to C9

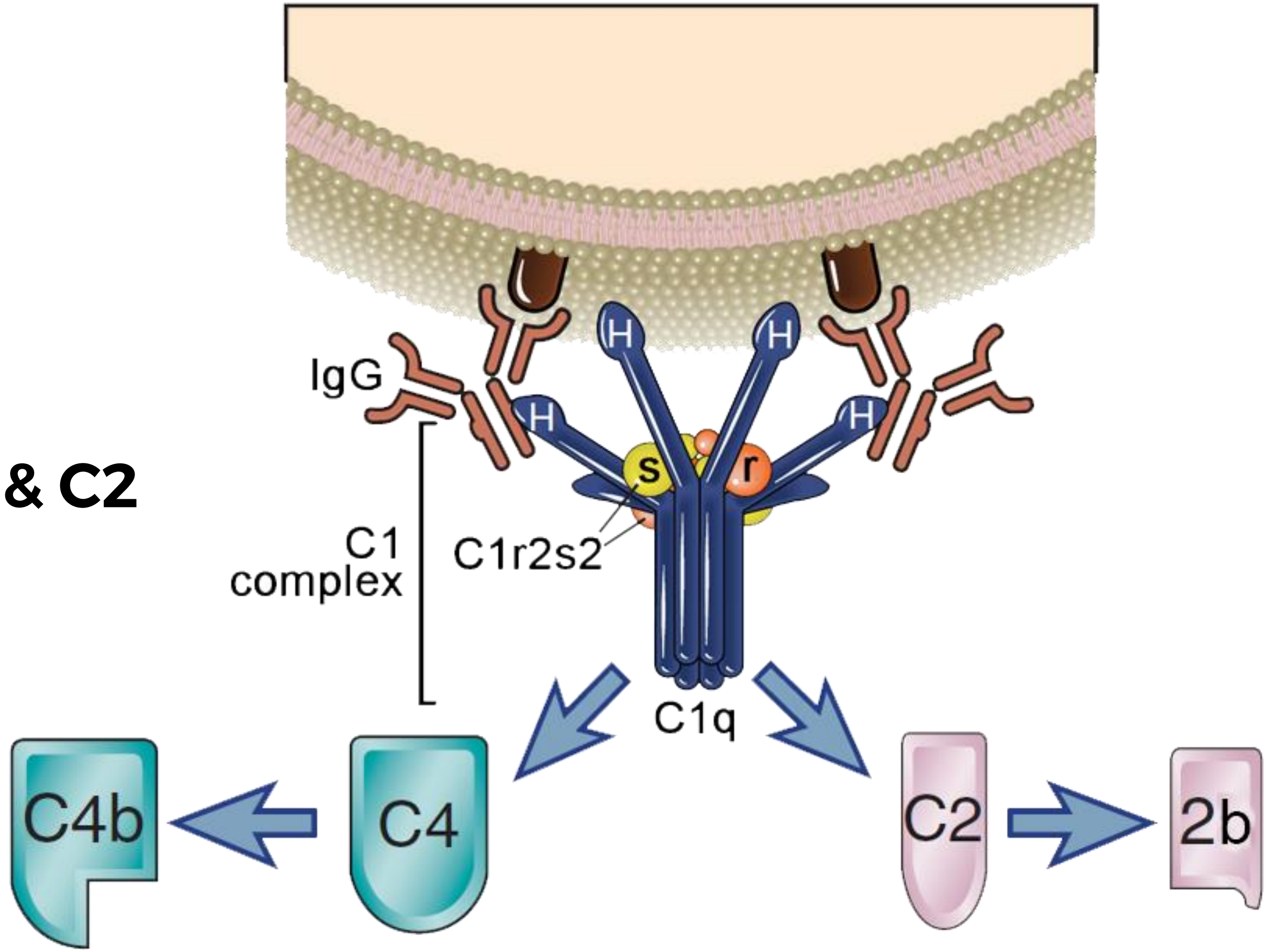


Classical pathway

➲ Initiation & 1st component activated

Ab: **IgM (most efficient) or IgG**

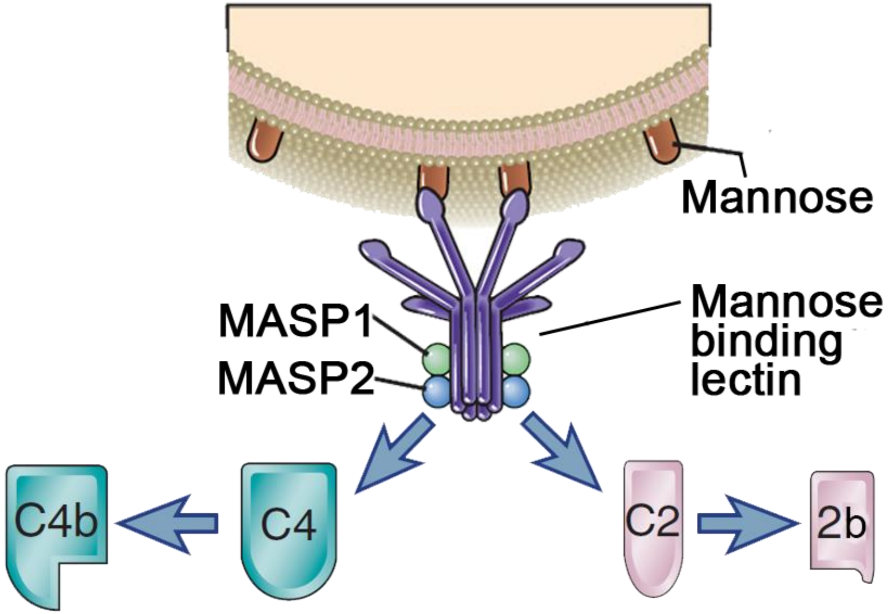
- ➥ Binds **Microbial (Ag) surface**
  - ➥ Interaction with **C1q**
    - ➥ **⊕ C1r & C1s**
      - ➥ C1qrs **cleaves C4& C2**



Lectin pathway

➲ Type of immunity

Innate immunity by microbes (bacteria) without Ab



➲ Involved components

a) **C2 to C9**

b) **Mannose binding lectin (MBL)**

➲ Initiation & 1st component activated

Mannose binding lectin (MBL) [similar in structure to C1qrs]

➥ Binds **polysaccharide (mannose) on bacterial surface**

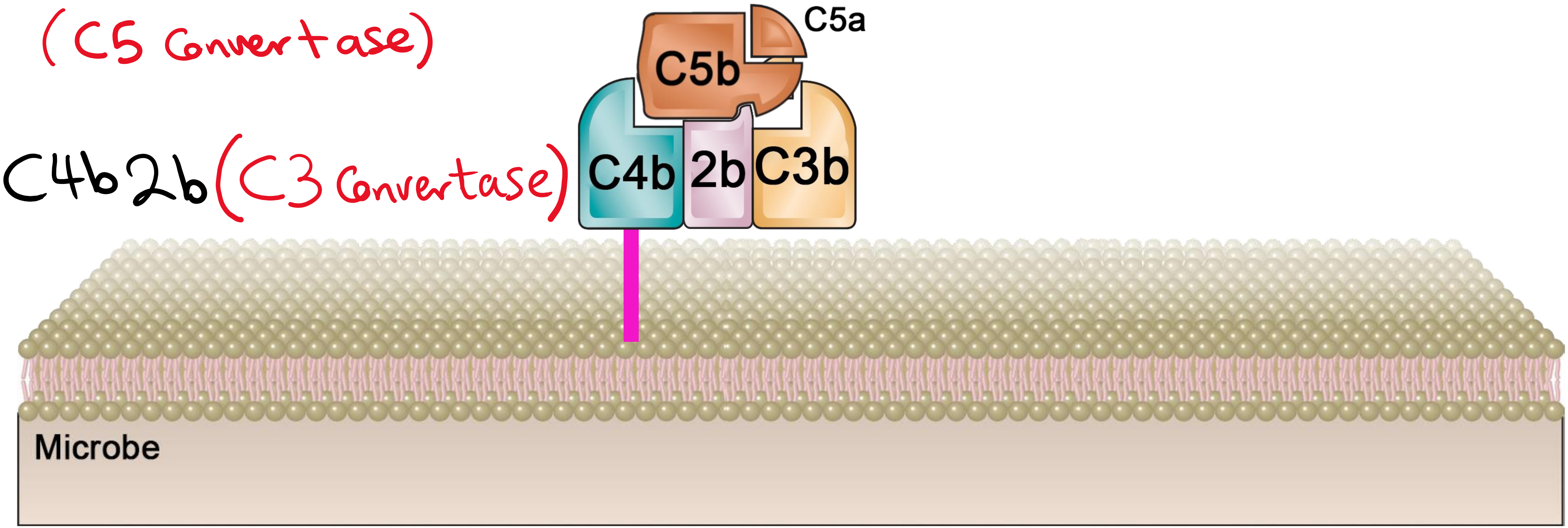
➥ **Cleavage of C4 & C2**

Classical pathway

Lectin pathway

C4b2bC3b
(C5 Convertase)

C4b2b (C3 Convertase)



Alternative pathway

➲ Type of immunity

Innate immunity by

Microbes (bacteria & fungi) without Ab

➲ Involved components

a) **C3,C5 to C9**

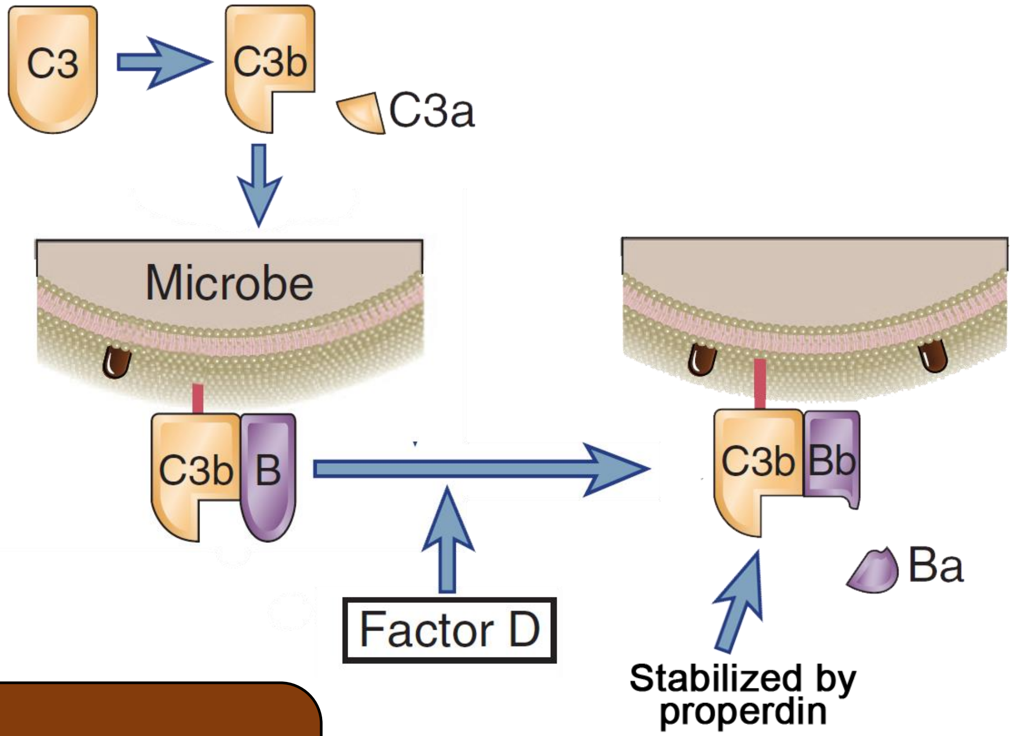
b) **Factor B, D & Properdin (P)**

➲ Initiation & 1st component activated

Spontaneous cleavage of C3

➥ **C3b** binds microbial surface

➥ **Factor B , D & Properdin** binds **C3b**



Classical pathway	Lectin pathway

➲ MAC : Membrane attack complex (Common final pathway)

C5b binds **C6,7,8 & multiple molecules of C9 (polymerized)**

↓

C5b6789 : **MAC**

↓

Pores in target membrane

↓

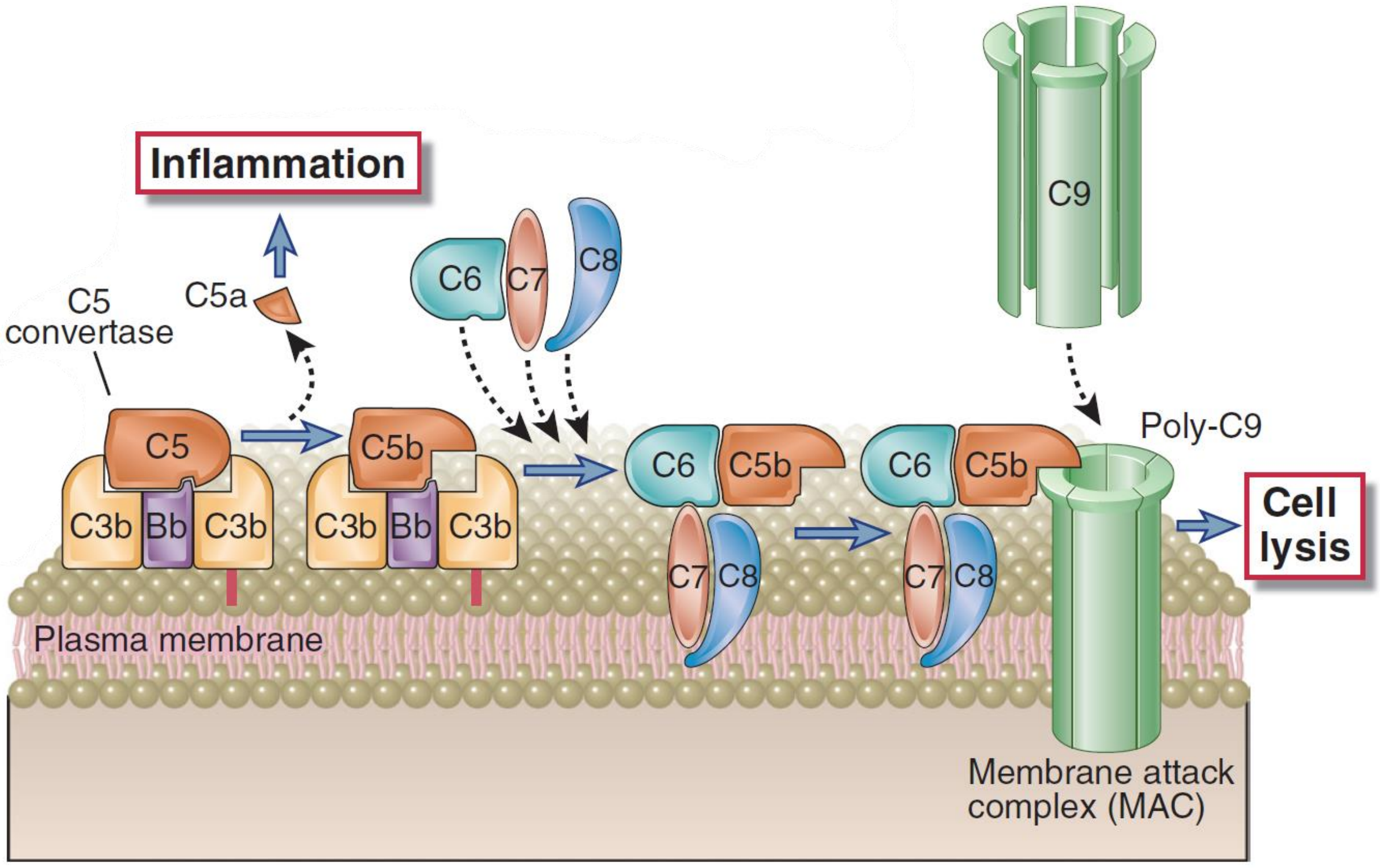
Entry of water

↓

Osmotic swelling

↓

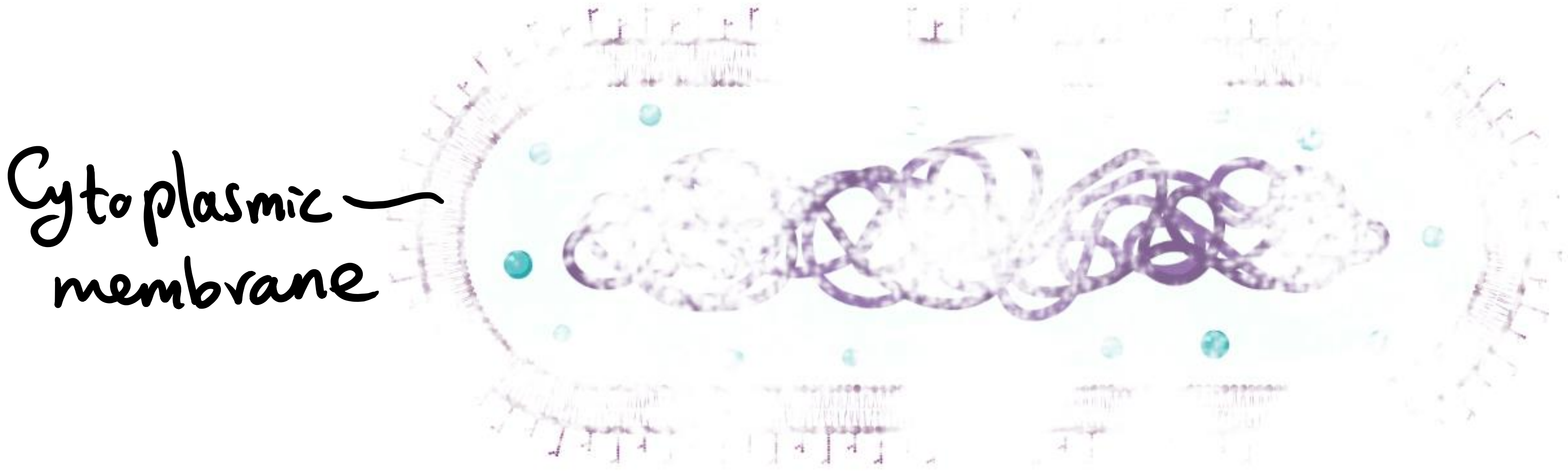
Lysis of target



	Classical pathway	**Lectin pathway**	**Alternative pathway**
Type of immunity	**Humoral (Adaptive)** immunity	**Innate** immunity by microbes (bacteria) without Ab	**Innate** immunity by microbes (bacteria & fungi) without Ab
Involved components	**C1 to C9**	a) **C2 to C9** b) **Mannose binding lectin (MBL)**	a) **C3,C5 to C9** b) **Factor B, D & Properdin (P)**
Initiation & 1st activated component	**Ab: IgM (most efficient) or IgG** → Binds **Microbial (Ag) surface** → Interaction with **C1q** → ⊕ **C1r & C1s** → C1qrs **cleaves C4& C2**	**Mannose binding lectin (MBL)** [similar in structure to C1qrs] ➥ Binds **polysaccharide (mannose) on bacterial surface** → ⊕ of 2 associated proteases: ➥ **Cleavage of C4 & C2**	**Spontaneous cleavage of C3** ➥ **C3b** binds microbial surface ➥ **Factor B ,D & Properdin** bind **C3b**
C3 convertase	**C4b2b (Cleaves C3)**		
C5 convertase	**C4b2b3b (Cleaves C5)**		
MAC : Membrane attack complex (Common final pathway)	C5b binds **C6,7,8 & multiple molecules of C9 (polymerized)** ↓ C5b6789 : **MAC** ↓ **Pores** in target membrane ↓ Entry of water ↓ Osmotic swelling ↓ **Lysis of target**		

I - Cytolysis : by C5b6789 (MAC)

Insertion of **MAC (C5b6789)** into cell membrane → Lysis of **organisms**



II- Stimulation of inflammatory response

A) Anaphylaxis : by anaphylatoxins (C3a,4a&5a)

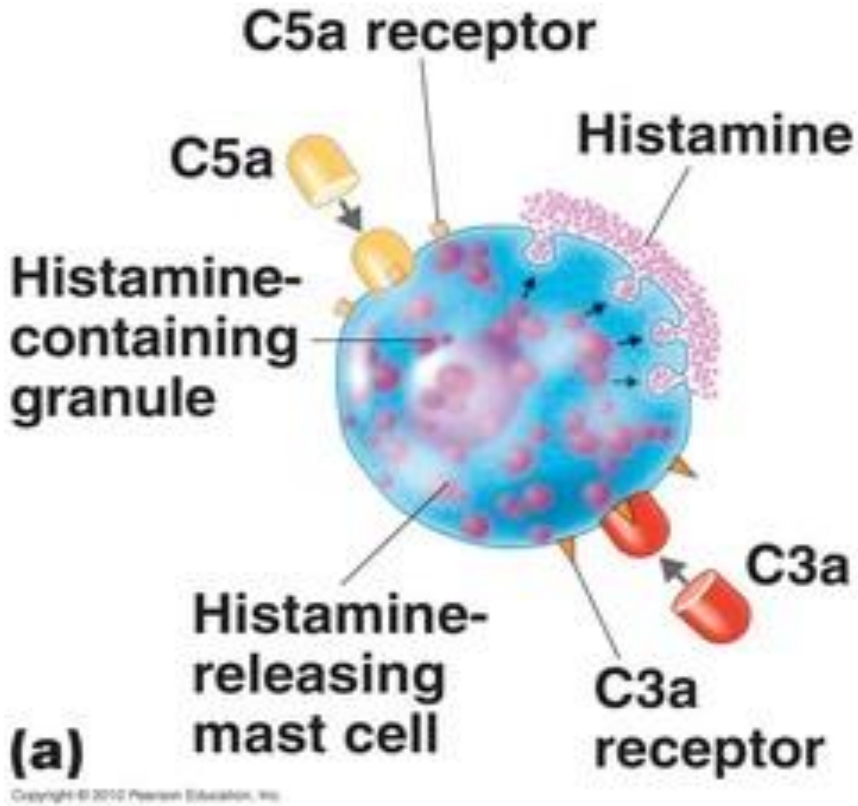
Attach to their **receptors on mast cells**

↓

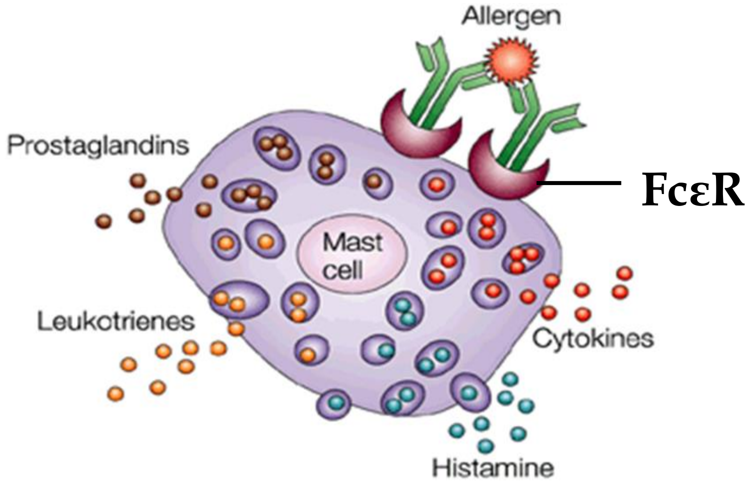
Degranulation & histamine release

↓

↑ **vascular permeability**



Mast cell has Fcε R for IgE

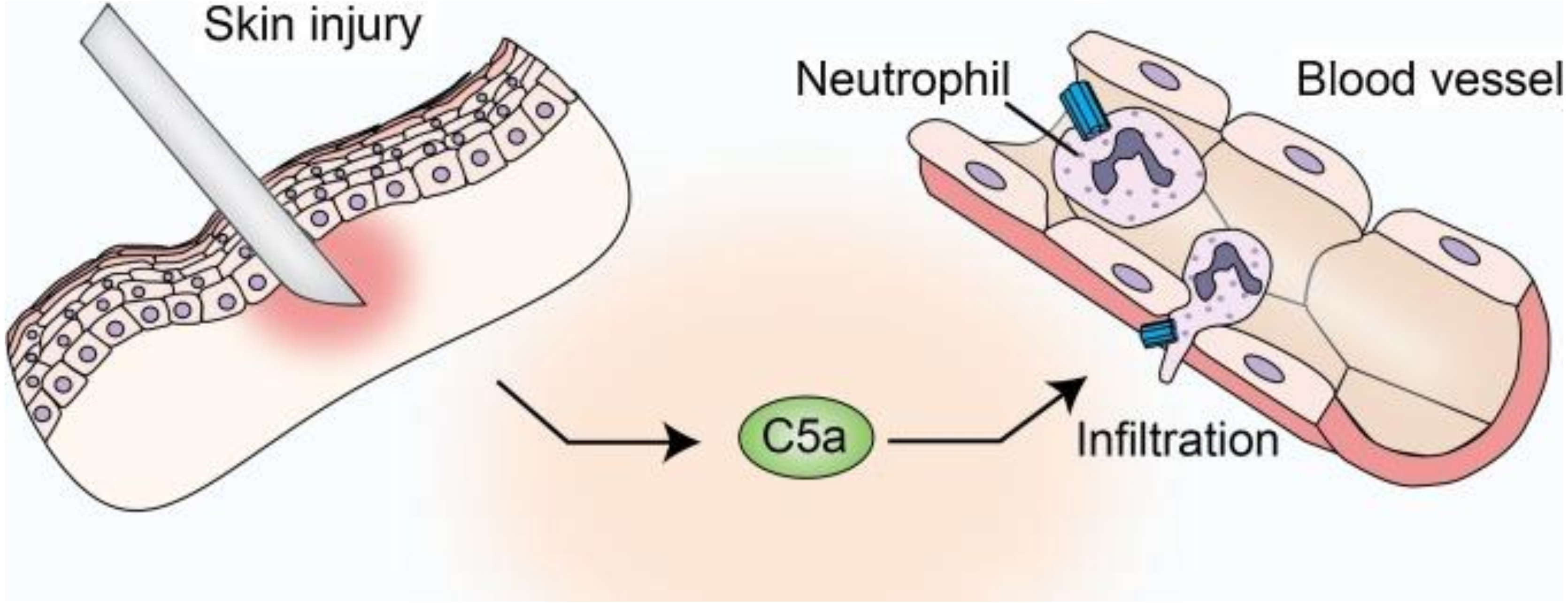


II- Stimulation of inflammatory response

B) Chemotaxis : by C5a

Attracts & recruits phagocytes (neutrophils)
to site of infection

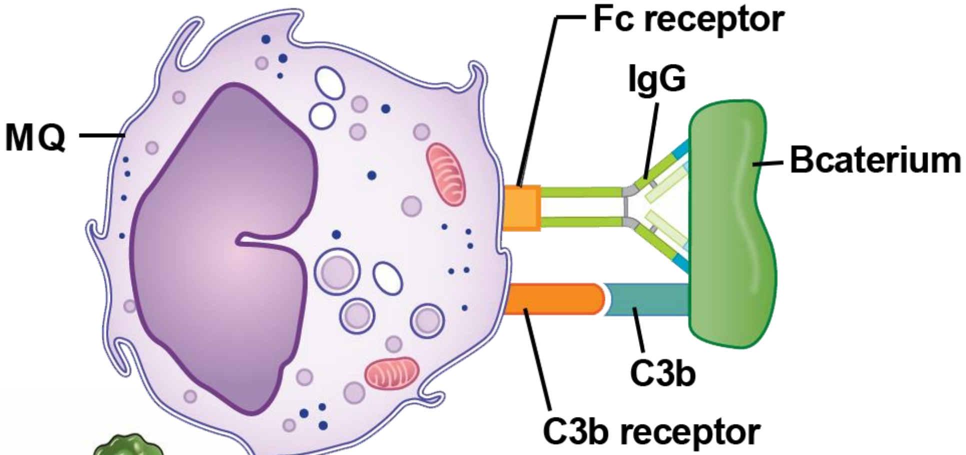
IL8 also causes chemotaxis

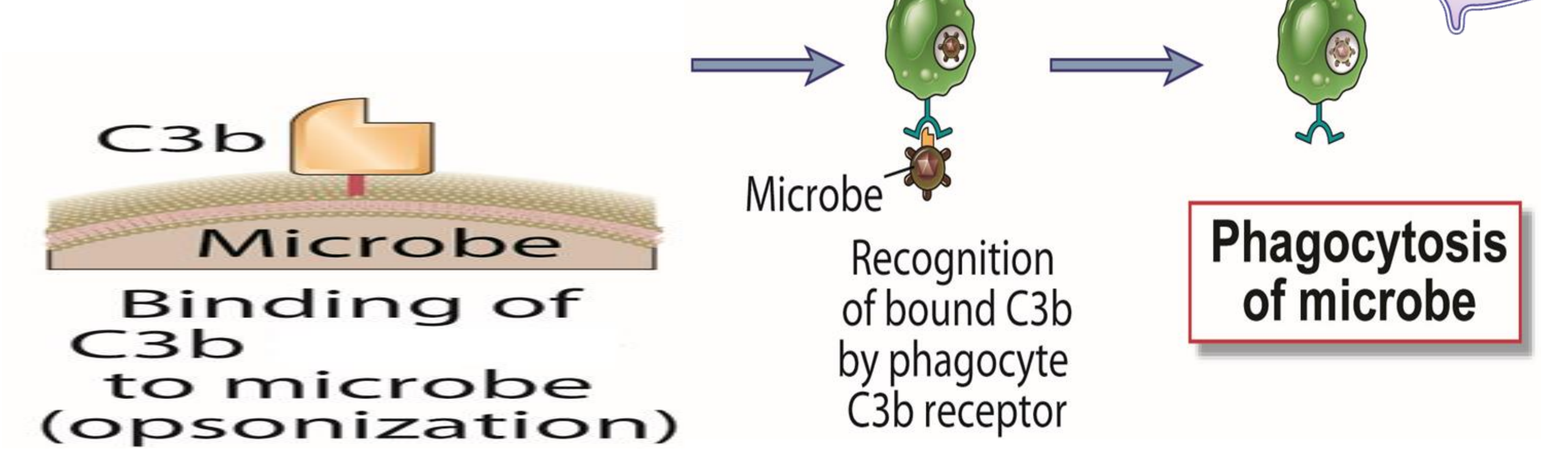


III- Opsonization & removal of immune complexes : by C3b

A) Opsonization

C3b coats **bacteria & viruses**
↓
Binds to **C3bR on phagocytes**
↓
Facilitates phagocytosis

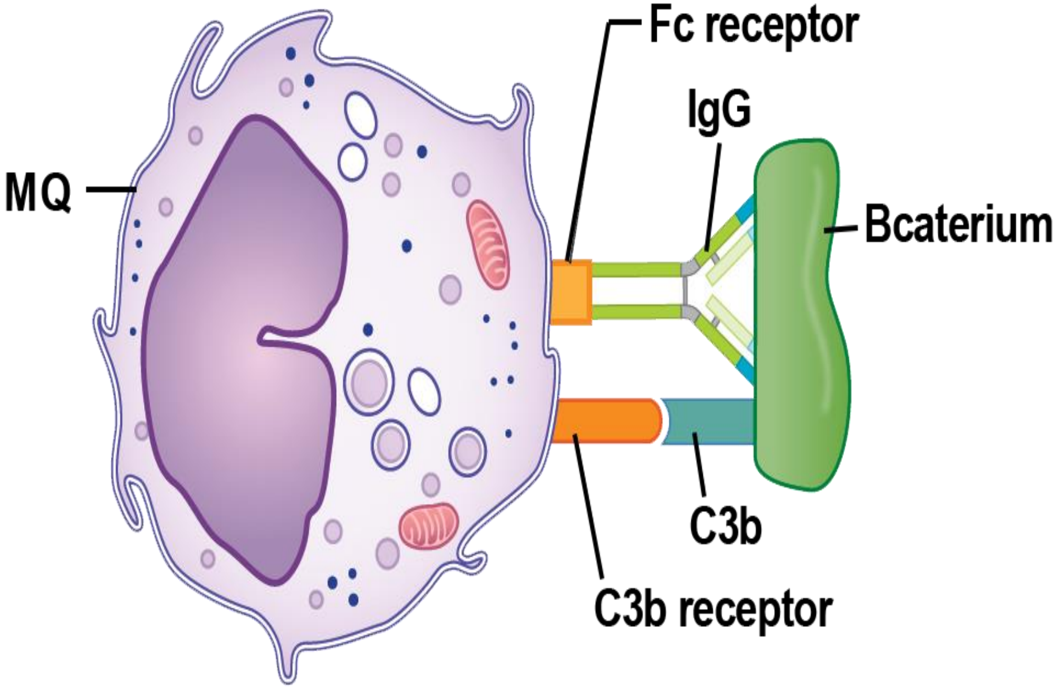



C3b
Microbe
Binding of C3b to microbe (opsonization)
Microbe
Recognition of bound C3b by phagocyte C3b receptor
Phagocytosis of microbe

B) Removal of harmful immune complexes

Opsonization (enhancement of phagocytosis)

Opsonins
- **Complement (C3b)**
- **Ab (IgG)**
- **Acute phase proteins**
  - Mannose binding lectin



Quiz 1

Which of the following complement components is an anaphylatoxin?

A. C1

B. C2a

C. C2b

D. C3a

E. C3b

Regulation of complement activation

كيف تمنع اضرار تنشيط Complement

I- Sialic acid on surface of self cells

II- Serum proteins

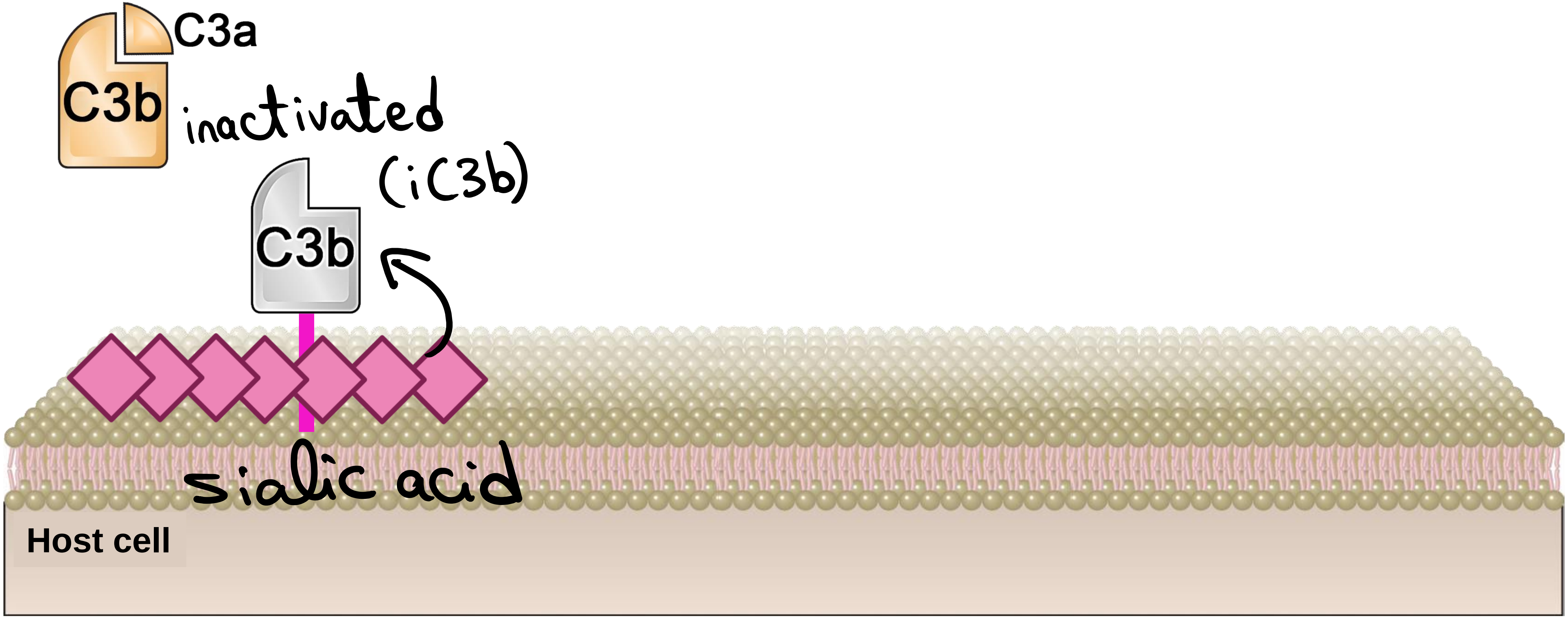
بروتينات في الدم

↑↑ levels of sialic acid on mammalian cells

الثدييات

Rapid inactivation of bound C3b

on host cells



Regulation of complement activation

II- Serum proteins

a) C1 inhibitor

Binds C1

↓

⊖ activation of classical pathway